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Exploratory analysis of chromophobe renal cell carcinoma in the SUNNIFORECAST trial comparing Ipilimumab plus Nivolumab vs standard of care as first-line treatment

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Background

Non-clear cell renal cell carcinomas (nccRCC) are a group of more than 20 histological and molecular defined entities. Chromophobe RCC (chRCC) are the second largest subgroup. Due to their rarity, treatment strategies are unclear and recommendations include TKI-, mTOR- or ICI-based therapies. We report the exploratory subgroup analyses of chRCC in the SUNNIFORECAST trial with ipilimumab/nivolumab (I/N) versus standard of care (SOC) 2016-000706-12, NCT03075423.

Methods

Pts with nccRCC were randomly assigned 1:1 to receive either ipilimumab 1 mg/kg IV plus nivolumab 3 mg/kg IV every 3 weeks (q3w) for 4 doses followed by a flat dose of nivolumab 240 mg IV q2w or 480 mg IV q4w versus SOC until disease progression. Pts were stratified according to IMDC score and papillary vs non-papillary histology. Central pathology according to the WHO classification 2022 was mandatory. The primary endpoint was the overall survival (OS)-rate at 12 months (mos), secondary endpoints were OS, progression free survival (PFS) and overall response rate (ORR). PD-L1 expression analysis was done exploratory.

Results

A total of 309 pts were randomized. Of these, 59 pts had chRCC (27/59 I/N, 32/59 SOC [TKI monotherapy, TKI/ICI or other]). The 12-mos-OS rate was higher with I/N than with SOC (88.9% vs 79.1%; p=0.16). Median OS was 40.2 mos (I/N) vs 36 mos (SOC) (HR 0.77; p=0.50). Of 55 pts evaluable for response, 26.9% with I/N vs 10.3% with SOC had a partial remission. mPFS was similar in both treatment arms (I/N 5.5 mos vs SOC 5.7 mos, HR 1.01; p=0.98). Notably, pts with a CPS > 1 (19/55 pts) had a significantly better 12-mos OS rate (83.3% vs 34.3%, p=0.014), mOS (45.3 mos vs 10.6 mos, HR 0.27 p=0.051) and ORR (41.7% vs 0% with I/N vs SOC). In contrast, chRCC pts with CPS <1 (36/55 pts) had a longer PFS with SOC (5.1 mos I/N vs 8.6 mos SOC, HR 1.41; p=0.41).

Conclusions

Exploratory analysis indicated a better 12-mos-OS rate, mOS and ORR in chRCC treated with I/N vs SOC especially in CPS > 1 pts. Conversely, chRCC pts with CPS < 1 seemed to benefit more from TKI. Our findings support the use of ICI-based therapies and suggest a possible role for PD-L1-testing in treatment decisions for nccRCC warranting further validation.

Clinical trial identification

2016-000706-12, NCT03075423.

Legal entity responsible for the study

University Hospital Frankfurt.

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Disclosure

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